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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Robert B Mondesi	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13,20-25 and 31-41* is/are pending in the application.

4a) Of the above claim(s) *13, 20-25 and 39-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-12 and 32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

4) ☐ Interview Summary (PTO-413)

DETAILED ACTION

Response to restriction requirement

Applicant's election with traverse of Invention Group I, **Claims 1-25, 28 and 31**, with a further election of core structure represented by structure 1d in Table 1, page 3, in amendment, filed March 3, 2004 is acknowledged. The traversal is on the ground(s) that the elected generic structure, while being a specific example of the structural formula Z-F-E-D-C-B-A-X, also reads on the structure formula of claim 1, Y-B-A-X where Y is Z-F-E-D-C resulting in Y-B-A-Z-F-E-D-C. This is not found persuasive because the elected core structure of the peptide of the invention is a peptide that consists of six amino acids. The general formula Y-B-A-X is drawn to a dipeptite and the general formula Z-C-B-A-X" is drawn to a tri peptide, the applicant has to shown nor is there evidence that the dipeptides and tripeptides of the invention have the same, structure, function or activity as the elected peptides that are consonant with the core structure of the compound of the invention (on page 73 of the specification peptide 1f (Table 1) has an IC50 of 800nm whereas the tripeptide 3-b (Table 2) on page 76 has IC50 of 1.4μm and dipeptide 7d (Table3) on page 88 has an IC50 of 6μm).

Furthermore the examiner would like to point out that new claims 39-41 are drawn to nonelected subject matter, method of inhibiting Hepatitis C virus, but will be rejoined with the product claims should the product claims be in a condition of allowability. "Guidance on Treatment of Product and Process Claims in light of *In*

re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Therefore the requirement is still deemed proper. **Claims 1, 5, 7 and 9** have been amended. **Claims 2, 14-19, 28-30** have been cancelled. **Claims 32-41** have been added. **Claims 1, 3-13, 20-25 and 31-41** are pending in this application. **Claims 13, 20-25, 31 and 39-41** are withdrawn from further consideration by the Examiner because these Claims are drawn to non-elected inventions. **Claims 1, 3-12 and 32-38** are currently under examination.

Information Disclosure Statement

The IDS filed March 3, 2004 has been received and is signed and considered, a copy of the IDS is attached to the following document.

Withdrawal of Objections and Rejections

Objection of specification for failure to provide sequence identifiers is withdrawn.

The objection of **claims 1 and 21** because of an informality is withdrawn.

The objection of **claims 2-16, 18-25, 28 and 31** because depending from a rejected base claim is withdrawn.

The objection of **claims 1-12, 18 and 19** because of sequence compliance rules is withdrawn.

The rejection of **claims 1, 17 and 29** under 35 U.S.C § 112, second paragraph is withdrawn.

The rejection of **claim 1** under 35 U.S.C § 102(b) as being anticipated by Hoss *et al.* is withdrawn.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-12 and 32-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds 1a-2c (Tables 1-2, Pages 73-74) and in the specification examples 1-6 (pages 44 -60), does not reasonably provide enablement for all the compounds presented by the general structure formula (I) of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue [illegible]

USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the

claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

In regards to the method of the invention and the breadth of the claims the broadest interpretation that applies is to compounds presented by the general structure formula (I) of claim 1.

2. The nature of the invention.

The invention is a novel class of pharmaceutical compounds that are inhibitors of Hepatitis C Virus (HCV) protease activity, specifically compounds that inhibit HCV NS3/NS4a serine protease activity.

3. The state of prior art.

In regards to the compounds of the invention presented by the general structure formula (I) of claim 1, the prior art does not provide any evidence of HCV protease inhibitory activity- specifically with regards to HCV NS3/NS4a serine protease inhibitory activity.

4. The relative skill in the art.

The relative skill in the art as it relates to pharmaceutical compounds that inhibit the activity of HCV serine protease is that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

Since the prior art does not teach that the compounds presented by general formula (I) of claim 1 formerly existed, the level of predictability is low in regards to the compounds of the invention with respect to HCV serine protease inhibitory activity. Therefore, one of skill in the art would not be able to readily anticipate the inhibitory effects of the compounds of the invention in view of HCV NS3/NS4a serine protease inhibitory activity.

6. The amount of guidance present.

The applicant has not provided guidance for all the compounds presented in the general formula (I) of claim 1. In tables 1-2 of the specification of the present application , the applicant has provided results of a HCV protease continuous assay for a group of compounds wherein the applicant has provided the IC50 values associated with each investigated compound as a barometer of HCV serine protease inhibitory activity. However, it is obvious to a person skill in the art that there is wide range of IC 50 values that is associated with these compounds, for example compound 1j has an IC50 value of 600nm whereas 1h has an IC50 value of 3 μm. With such an apparent wide range of HCV protease activity it is pertinent that the applicant discloses further experimentation to show a person skill in the art the level of potency for a given compound of the invention. Such information is required by a person skill in the art in order to be

able to use the correct amount of the compound of the invention in a process such as an assay or a method of treatment. Furthermore the applicant has only shown how to make a handful of the peptides of the invention, compound 1a, 1b, 1c, 1d and 2a (examples 1-6), since the general structure formula of claim 1 allows for a much larger number of possible peptides than disclosed, a person skill in the art would need more guidance as to how to make all the compounds presented by the general structure formula of claim 1. In view of the compounds of the invention, the applicant has shown some guidance as to how certain compounds of the invention, compounds 1a-2c (Tables 1-2, Pages 73-74) and in the specification examples 1-6 (Pages 44 -60) can be made and perhaps used to inhibit HCV protease activity - but the applicant has not provided guidance for all the compounds presented in the general structure formula (I) of claim 1 in regards to how they can be made and used to inhibit HCV serine protease activity.

7. The existence of working examples.

The specification, examples 1-6 (Pages 44-60) provides specific working examples of compounds (Tables 1-2) that can be used to inhibit HCV serine protease activity. However, the specification does not provide working examples of all compounds suggested by the general structure formula (I) of claim 1.

8. The quantity of experimentation necessary.

In the case of using all the compounds suggested by the general structure formula (I) of claim 1, a large quantity of experimentation needs to be disclosed in order for a person skill in the art to be able to practice the invention, since

there are a multitude of possible compounds that are suggested by the general structure formula of claim 1 and each compound needs to be tested for HCV protease inhibitory activity.

Due to the quantity of experimentation still required to be performed by one skill in the art in regards to how to use all the compounds suggested by the general formula (I) of claim 1, the lack of guidance presented in the specification regarding the same, the absence of a working example directed to same, the unpredictable nature of the invention with regards to HCV serine protease inhibitory activity, the state of the prior art not providing any evidence that all the compounds suggested by general formula (I) of claim 1 will exhibit HCV serine protease inhibitory activity , and the breath of the claims which fails to provide particular steps for all compounds suggested by the general formula (I) of claim 1 exhibiting HCV serine protease inhibitory activity, the specification fails to teach the skilled artisan in the art how to make and use the invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBM

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04-12-04

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